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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicant(s): Alan P. Kozikowski *et al.*

Examiner: Celia C. Chang

Application No.: 10/576,620

Art Unit: 1625

Filed: March 8, 2007

Atty. Docket No.: **GUX-010.01**

Title: *Dopamine-, Norepinephrine-, and  
Serotonin-Transporter-Selective  
Heterocyclic Compounds and Their  
Therapeutic Applications*

Confirmation No: 4324

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**AMENDMENT & RESPONSE**

Dear Examiner Chang:

In response to the Final Office Action in the above-identified application, which was dispatched on August 26, 2011, the Applicants submit this paper. No new matter has been added.

**Amendments to the Claims** begin on page 2.

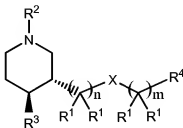
**Remarks** begin on page 8.

EXAMINER'S AMENDMENT

~~CLAIMS~~

This listing of the claims will replace all prior versions and listings of the claims in the application.

1. **(currently amended)** A compound represented by formula I:



I

wherein

$R^1$  represents independently for each occurrence H or alkyl;

$R^2$  is H, alkyl, aryl, aralkyl, or  $-C(O)R^5$ ;

$R^3$  is <sup>optionally substituted</sup> aryl, heteroaryl, or aralkyl;

$R^4$  is hydrogen, hydroxyl, aryl, heteroaryl,  $OR^5$ ,  $CO_2R^6$ ,  $C(O)N(R^6)_2$ ,  $C(O)NHOH$ ,  $OC(O)R^5$ , or oxadiazole;

$R^5$  is alkyl, aryl, heteroaryl, or aralkyl;

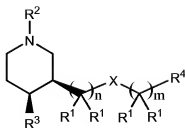
$R^6$  represents independently for each occurrence hydrogen, alkyl, aryl, or aralkyl, wherein any two instances of  $R^6$  may be covalently attached to form a ring;

X is S,  $-S(O)-$ , or  $-S(O)_2-$ ;

n is 1, 2, 3, or 4; and

m is 1, 2, 3, or 4.

2. **(currently amended)** A compound represented by formula II:



II

wherein

R<sup>1</sup> represents independently for each occurrence H or alkyl;

R<sup>2</sup> is H, alkyl, aryl, aralkyl, or -C(O)R<sup>5</sup>;

R<sup>3</sup> is ~~aryl~~ optionally substituted heteroaryl, or aralkyl;

R<sup>4</sup> is ~~hydrogen, hydroxyl, aryl, heteroaryl, OR<sup>5</sup>, -CO<sub>2</sub>R<sup>6</sup>, C(O)N(R<sup>6</sup>)<sub>2</sub>, C(O)NHOH, OC(O)R<sup>5</sup>, or oxadiazole;~~

R<sup>5</sup> is alkyl, aryl, heteroaryl, or aralkyl;

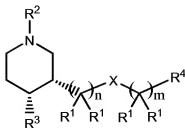
R<sup>6</sup> represents independently for each occurrence hydrogen, alkyl, aryl, or aralkyl, wherein any two instances of R<sup>6</sup> may be covalently attached to form a ring;

X is S, -S(O)-, or -S(O<sub>2</sub>)-;

n is 1, 2, 3, or 4; and

m is 1, 2, 3, or 4.

3. **(currently amended)** A compound represented by formula III:



III

wherein

$R^1$  represents independently for each occurrence H or alkyl;

$R^2$  is H, alkyl, aryl, aralkyl, or  $-C(O)R^5$ ;

$R^3$  is  $\text{optionally substituted}$   
 aryl, heteroaryl, or aralkyl;

$R^4$  is ~~hydrogen, hydroxyl, aryl, heteroaryl, OR<sup>5</sup>, CO<sub>2</sub>R<sup>6</sup>, C(O)N(R<sup>6</sup>)<sub>2</sub>, C(O)NHOH,~~  
 $\text{OC(O)R}^5$ , or oxadiazole;

$R^5$  is alkyl, aryl, heteroaryl, or aralkyl;

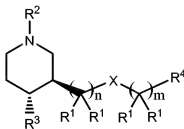
$R^6$  represents independently for each occurrence hydrogen, alkyl, aryl, or aralkyl,  
 wherein any two instances of  $R^6$  may be covalently attached to form a ring;

X is S,  $-S(O)-$ , or  $-S(O)_2-$ ;

n is 1, 2, 3, or 4; and

m is 1, 2, 3, or 4.

4. **(currently amended)** A compound represented by formula IV:



IV

wherein

$R^1$  represents independently for each occurrence H or alkyl;

$R^2$  is H, alkyl, aryl, aralkyl, or  $-C(O)R^5$ ;

$R^3$  is  $\text{optionally substituted}$   
 aryl, heteroaryl, or aralkyl;

$R^4$  is ~~hydrogen, hydroxyl, aryl, heteroaryl, OR<sup>5</sup>, CO<sub>2</sub>R<sup>6</sup>, C(O)N(R<sup>6</sup>)<sub>2</sub>, C(O)NHOH,~~  
 $\text{OC(O)R}^5$ , or oxadiazole;

$R^5$  is alkyl, aryl, heteroaryl, or aralkyl;

R<sup>6</sup> represents independently for each occurrence hydrogen, alkyl, aryl, or aralkyl, wherein any two instances of R<sup>6</sup> may be covalently attached to form a ring;

X is S, -S(O)-, or -S(O)<sub>2</sub>-;

n is 1, 2, 3, or 4; and

m is 1, 2, 3, or 4.

Claims 5-23 (canceled)

<sup>5</sup>  
~~24.~~ (original) The compound of claim 2, wherein X is S or -S(O)-.

<sup>6</sup>  
~~25.~~ (original) The compound of claim 2, wherein R<sup>2</sup> is methyl, ethyl or propyl.

<sup>7</sup>  
~~26.~~ (original) The compound of claim 2, wherein R<sup>2</sup> is methyl.

<sup>8</sup>  
~~27.~~ (currently amended) The compound of claim 2, wherein R<sup>3</sup> is ~~aryl~~ <sup>optionally</sup> substituted phenyl ~~optionally~~ substituted phenyl.

<sup>9</sup>  
~~28.~~ (currently amended) The compound of claim <sup>8</sup>[[2]] ~~27~~, wherein R<sup>3</sup> is halophenyl.

<sup>10</sup>  
~~29.~~ (currently amended) The compound of claim <sup>8</sup>[[2]] ~~27~~, wherein R<sup>3</sup> is 3-chlorophenyl.

30. (canceled)

<sup>11</sup>  
~~31.~~ (currently amended) The compound of claim 2, wherein ~~R<sup>4</sup> is C(O)N(R<sup>6</sup>)<sub>2</sub> and R<sup>6</sup>~~ represents independently for each occurrence hydrogen or alkyl.

<sup>12</sup>  
~~32.~~ (original) The compound of claim 2, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, and R<sup>3</sup> is 3-chlorophenyl.

33. (canceled)

<sup>13</sup>  
~~34.~~ (original) The compound of claim 2, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, R<sup>3</sup> is 3-chlorophenyl, and R<sup>4</sup> is C(O)N(H)iPr.

<sup>14</sup>  
~~35.~~ (original) The compound of claim 3, wherein X is S or -S(O)-.

<sup>15</sup>  
~~36.~~ (original) The compound of claim 3, wherein R<sup>2</sup> is methyl, ethyl or propyl.

<sup>16</sup>  
~~37.~~ (original) The compound of claim 3, wherein R<sup>2</sup> is methyl.

17  
38. (currently amended) The compound of claim 3, wherein R<sup>3</sup> is ~~aryl~~ optionally substituted phenyl <sup>17</sup> ~~aryl~~ <sup>17</sup> ~~optionally~~ substituted phenyl.

18  
39. (currently amended) The compound of claim [[3]] <sup>17</sup> ~~38~~, wherein R<sup>3</sup> is halophenyl.

19  
40. (currently amended) The compound of claim [[3]] <sup>17</sup> ~~38~~, wherein R<sup>3</sup> is 3-chlorophenyl.

41. (canceled)

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42. (currently amended) The compound of claim 3, wherein R<sup>4</sup> is C(O)N(R<sup>6</sup>)<sub>2</sub> and R<sup>6</sup> represents independently for each occurrence hydrogen or alkyl.

21  
43. (original) The compound of claim 3, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, and R<sup>3</sup> is 3-chlorophenyl.

44. (canceled)

22  
45. (original) The compound of claim 3, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, R<sup>3</sup> is 3-chlorophenyl, and R<sup>4</sup> is C(O)N(H)iPr.

23  
46. (original) The compound of claim 4, wherein X is S or -S(O)-.

24  
47. (original) The compound of claim 4, wherein R<sup>2</sup> is methyl, ethyl or propyl.

25  
48. (original) The compound of claim 4, wherein R<sup>2</sup> is methyl.

26  
49. (currently amended) The compound of claim 4, wherein R<sup>3</sup> is ~~aryl~~ optionally substituted phenyl <sup>26</sup> ~~aryl~~ <sup>26</sup> ~~optionally~~ substituted phenyl.

27  
50. (currently amended) The compound of claim [[4]] <sup>26</sup> ~~49~~, wherein R<sup>3</sup> is halophenyl.

28  
51. (currently amended) The compound of claim [[4]] <sup>26</sup> ~~49~~, wherein R<sup>3</sup> is 3-chlorophenyl.

52. (canceled)

29  
53. (currently amended) The compound of claim 4, wherein R<sup>4</sup> is C(O)N(R<sup>6</sup>)<sub>2</sub> and R<sup>6</sup> represents independently for each occurrence hydrogen or alkyl.

30  
54. (original) The compound of claim 4, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, and R<sup>3</sup> is 3-chlorophenyl.

55. (canceled)

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~~36.~~ (original) The compound of claim 4, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, R<sup>3</sup> is 3-chlorophenyl, and R<sup>4</sup> is C(O)N(H)iPr.

Claims 57-107(canceled)

32

~~108.~~ (previously presented) The compound of claim 1, wherein X is S or -S(O)-.

33

~~109.~~ (previously presented) The compound of claim 1, wherein R<sup>2</sup> is methyl, ethyl or propyl.

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~~110.~~ (previously presented) The compound of claim 1, wherein R<sup>2</sup> is methyl.

35

~~111.~~ (currently amended) The compound of claim 1, wherein R<sup>3</sup> is <sup>optionally</sup> ~~substituted phenyl~~ <sup>aryl optionally</sup> substituted phenyl.

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~~112.~~ (currently amended) The compound of claim <sup>35</sup> ~~[[1]]~~ <sup>111</sup>, wherein R<sup>3</sup> is halophenyl.

37

~~113.~~ (currently amended) The compound of claim <sup>35</sup> ~~[[1]]~~ <sup>111</sup>, wherein R<sup>3</sup> is 3-chlorophenyl.

114. (canceled)

38

~~115.~~ (currently amended) The compound of claim 1, wherein ~~R<sup>4</sup> is C(O)N(R<sup>6</sup>)<sub>2</sub>~~ and R<sup>6</sup> represents independently for each occurrence hydrogen or alkyl.

39

~~116.~~ (previously presented) The compound of claim 1, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, and R<sup>3</sup> is 3-chlorophenyl.

117. (canceled)

40

~~118.~~ (previously presented) The compound of claim 1, wherein X is S, n is 1, m is 1, R<sup>1</sup> is hydrogen, R<sup>2</sup> is methyl, R<sup>3</sup> is 3-chlorophenyl, and R<sup>4</sup> is C(O)N(H)iPr.